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Dr. William S. Stone

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A REVIEW OF THE HISTORY OF CHEMICAL THERAPY IN CANCER.

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BY

WILLIAM S. STONE, M.D. NEW YORK.

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A REVIEW OF THE HISTORY OF CHEMICAL THERAPY IN CANCER.

BY WILLIAM S. STONE, M.D.,

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THE presentation of a method of cancer therapy other than operation with the knife has usually been conceived either in ignorance or in the hope of financial gain. In the case of the chemical caustics, unfortunately for progress in the treatment of the disease, the unqualified condemnation of the manner of their exploitation has repeatedly prevented educated surgeons from learning how to use them and excluded a scientific study of their possible efficiency.

It is a remarkable fact that, so far as "cancer cures" relate to the local treatment of the disease, they have almost invariably been found to consist of arsenic, zinc, or the alkaline caustics. Arsenic is known to have been the effective ingredient of the applications made to cancerous tumors by the Indians, Egyptians, and Persians, and a salve, designated as Unguentum Egypticum, consisting of arsenic and vinegar, was in general use until the middle of the fourteenth century, when two notable surgeons of the University of Avignon, Henri de Mondeville and Guy de Chauliac, made ef-

forts to improve the methods of diagnosis and treatment. Prior to this period it is clear that all classes of people-physicians, scholars, mendicant friars, and old women—treated all kinds of tumors with escharotic pastes and solutions, the most effective of which contained arsenic. The most skillful applications were undoubtedly made by the The Hippocratic theory of the nature of cancer, "the atra bilis," was recognized in all therapeutic efforts, but exerted little influence on the methods of treatment. Diagnostic error, as a factor in the determination of successful results, applied alike to the use of the knife and to caustics. While Galen and others of the Greek school supported this theory, two kinds of growth were differentiated: (1) the so-called scirrhus, which evidently included both benign tumors and the hard, slowly growing, and more definitely localized malignant growths; (2) those growths which were plainly evident to both patients and physicians as the more rapidly growing and destructive neoplasms. It is probable that chemical caustics were more generally used than either the knife or the heated iron, especially with the ulcerating growths.

Guy de Chauliac (1368), a great writer on surgery, as well as a skillful operator, directed attention to the use of caustics as an adjuvant to the use of the knife. He used arsenic mixed with clay and noted no toxic symptoms from its employment. Ambroise Paré (1510-1590), by his development of the use of ligatures and sutures, created a fresh enthusiasm for the use of the knife in the treatment of cancer, and, although using mild salves and solutions on ulcerating growths, tried to discredit the use of arsenic because of the baleful effects of its indiscriminate application. In Germany, Fabricius

Hildanus (1560-1634), who was known as a skillful operator, and is reported to have excised the axillary glands in amputation of the breast, also tried to discredit the use of arsenic. We find, however, little evidence during the succeeding centuries that surgery profited much by the possibilities which the work of Paré and Fabricius had indicated. Clowes, physician to Queen Elizabeth, advocated as an additional therapeutic procedure the laying on of the Queen's hand. In Germany, theories regarding the nature of cancer simply became more numerous, and under the designation of "systems" their chief practical achievement was the exploitation of a constitutional cure in the form of conium maculatum by a Dr. Störck of Vienna, in 1761, an account of which eleven years later extolled its merits and the discoverer in terms of the highest praise. In 1779 a society in Bantzen offered a prize of 30 ducats for a cure of cancer without the use of the knife, mercury, cicuta, stramonium, belladonna, napello, and aconite, but there is no record of any award of the prize. In France the efforts to apply the recent discoveries in chemistry to the study of the nature of cancer had elicited the fact that tumors arise from the same tissue in which they appear. In 1773 Bernard Peyrilhe, in a thesis offered for the prize question by the Academy of Lyons, "Qu'est-ce le cancer," presented a scientific interpretation of the subject, and is credited with being the first to make use of animal experimentation in the study of the disease. The dog, however, into whose back the cancerous material had been injected, howled so continuously from the resulting lesion that its keeper removed him from the field of Peyrilhe's observations. In regard to treatment, he recommended for cancer of the breast the removal of the breast, excision of the axillary glands, and the removal of the pectoralis major muscle. For the treatment of nasal cancer he advocated the use of the recently discovered "kohlsäure."

The beginning of the nineteenth century was marked by efforts to overthrow ancient philosophy and medieval empiricism, and a new era in the conception and treatment of cancer appeared through the English and French anatomical researches. While John Hunter's (1786) lymphatic theory dominated the minds of the majority of the great surgeons, it included a new conception of cancerous growths as being the result of some vital activity on the part of normal tissues and subject to the same laws of life, growth and nourishment as the normal organism. In London (1771) the Middle-sex Hospital had established a special ward for cancer patients, and in 1802 a committee of London surgeons was formed for the investigation of the nature and cure of cancer. During the three years of its existence its chief attainment was the distribution to the medical profession in England of an elaborate questionnaire, the result of which was as futile as it probably would be to-day if a similar method was pursued. Among the practical surgeons there were two factions regarding the theory of cancer—the "localists" and the "constitutionalists." The latter did not hold to a specific theory. but their ranks were largely derived from the orthodox surgeons of the day who had been so uniformly disappointed with the results of their operative work.

A publication by Young in London appeared in 1805 on cancer and the use of chemical caustics in its treatment, in which a remarkably clear summary is given of the fallacious arguments of those who

maintained that cancer has a specific virus, is contagious or hereditary, and its action constitutional. His own conception of cancer presents with astonishing accuracy the present views of scientific men. "Morbid and natural structures, having the same principle necessary to each and governing both," he says, "a morbid alteration should never be viewed independently of the natural organization and functions of the part, or as beyond the laws of life." Briefly summarized, he considers cancer as a growth arising from acquired actions about a local structure that has been altered by injury or disease. On the recurrence of cancer, he says: "It must be obvious that the disease arises from such small beginnings, unfortunately, that it can never be detected until the obstruction has made considerable progress; and, as no specific virus is with it so as to offer any peculiar evidence from which one might take alarm, the disease thus proceeds securely in the minute parts of structure until such a circle of alteration is acquired as to make the change evident to the touch; so that when a surgeon takes out such a scirrhus tumor it is impossible to act beyond the reach of his perceptions, and to discover changes which can only be imagined, which may be there, or may not. . . . It is impossible to ascertain the distinct line between health and disease. and . . . some portions may be left, from which . . . the disease may ultimately recur."

Based upon this conception of the disease, Young directed the attention of the educated physician to the advantages which he believed the chemical caustics possessed if they were more discriminately and skillfully applied. He says: "It must be very evident to the most sanguine expectations that this disease, although the treatment of it in the future

may be greatly improved, must still, in many instances, fall short of all possibility of cure. But . . . are we to relax in effort because effort is more required? Shall we withhold what can be done, merely because all that we wish cannot be done? Such, however, seems to have been the desperate sentiment in which science has left the disease almost to itself. It appears to have been considered as a thing so deeply rooted in its own sin and wickedness as to be beyond reprieve—a hardened malefactor, denied every consolation but that of the knife. This negligence on the part of science has given proportionate scope to the invention of the quacks: they have seized upon the arms the regulars threw away, and have certainly played no unsuccessful part. Even old women, enlisted under the banners that were deserted, have proved at least (as far as their knowledge of the question went) that there is just as much orthodoxy in a piece of caustic as in a piece of iron."

As illustrating the attitude of the regular surgeon at that time toward the use of caustics, Young narrated the story of a published correspondence between two surgeons of the time. A regular surgeon, Mr. Guy, had purchased a nostrum, known as the "Plunket remedy," which he had been using extensively and apparently successfully without disclosing its composition, but claiming it had none of the qualities of a caustic. The surgeon to the King. Mr. Gataker, who, it afterward was ascertained, had also been using a caustic without the same success as had his colleague, publicly and vehemently denounced Mr. Guy because he was using a secret remedy. The efficient ingredient of the "Plunket remedy" was eventually ascertained to be arsenic. Young says: "Thus posterity seems equally obliged to these two gentlemen; to the one for condemning a thing which it is very evident he was totally ignorant; and to the other for the warm support of what it is equally clear he did not understand, or (which would seem still less innocent) of what he did not choose to understand." Young indicates that a more general use of caustics became introduced from this remedy, which considering the unqualified and indiscriminating way in which they were applied, were attended with more success, he says, than could have been looked for.

Young conceived that the advantage gained by the proper use of caustics was derived from their power of exciting newly formed tissues into an activity beyond their power, which is always less than normal structures. For this purpose he considered arsenic as particularly well suited because its action extended to all of the tumor tissue without rapidly producing a superficial eschar, the formation of which prevents the extension of the action to the deeper parts. An old preparation, known as Magnes Arsenicales, which he regarded as most efficacious, consisted of equal parts of antimony, sulphur, and arsenic, the antimony, he believed, adding to the extent of the area affected. Young urged the importance of applying treatment during the early stages of the disease, and, in order to avoid concealment of these tumors until it is too late, he writes as follows: "So long as the extirpation of scirrhi of the breast is performed by the knife, so long shall we have the disease fostered in secret, and, in too many instances, procrastinated beyond the point of safety, through the dread of an operation that is inevitably dreadful. For the operator may argue until doomsday ere he shall persuade his patient that cutting the breast with the knife is a mere nothing. . . . This rhetoric never gained a jot on the fears of ignorance, or on the quick feelings of diseased delicacy. The truth is that, when the operation is submitted to, the mind is seldom made up to it but as a last resort—seldomer from the convictions of reason, and never from an absolute command over the natural terrors of the heart."

There is no reason to doubt that Young's presentation of the subject had a favorable effect on the professional mind in both England and France. He was a graduate of the Middlesex Hospital, and, although not a member of the staff of that institution, he was a protege of Mr. Brodbeck, who made the first financial contribution to the establishment of its cancer ward. He became better known by a publication in 1815 on the treatment of cancer by compression, a method which received wide attention for many years. Récamier was enthusiastic about its efficacy, and devoted two volumes to a discussion of its principles and technical application.

From the beginning of the nineteenth century we find that all of the noted surgeons felt the need of some adjuvant to or substitute for the use of the knife, and until the last quarter of the century the use of caustics in cancer therapy was regularly discussed in the standard surgical textbooks. There are, however, few contributions to their technical application and very little discussion of the kind of cases to which they are applicable. Of all the noted surgeons of his time Velpeau seems to have made the most use of them, a paste designated as "caustique noir," consisting of concentrated sulphuric acid made into a paste, being his favorite formula. He says: "I have frequently employed caustics in the treatment of cancer, and I have fre-

quently thought, I must confess, that they have more certainly prevented secondary cancerous affections in the neighboring glands than the extirpation with the knife. I have twice seen voluminous and indurated glands in the axilla diminish in a remarkable degree during the period I was destroying a cancer of the breast by caustics, and I have observed the same effect on the submaxillary glands, while cancer . . . of the lower lip was treated in a similar manner." Maisoneuve also refers repeatedly to the efficiency of caustics, especially of the chloride of zinc, in the removal of cancerous tumors, and of the long interval before they recurred. Dupuytren, as a part of his armamentarium, used a paste consisting of two parts of arsenic and 200 parts of calomel, which Parker refers to as generally too feeble in its action. Manec, of the Salpêtrière Hospital, Paris, used a paste consisting of one part arsenous acid, eight parts of cinnibar, and four parts of burnt sponge, made into a paste with a few drops of water. The results from its use were favorably commented upon by Lebert, who, Parker says, was not an ardent advocate of caustics. All of these cases had been referred to Manec by other distinguished surgeons as incurable.

Sir Astley Cooper is quoted by Parker as follows: "It behooves medical men to direct their minds to the trial of the numerous agents which chemistry and botany have lately abundantly discovered and simplified." Most of the pastes used during the first third of the nineteenth century consisted either of arsenic or the mineral acids, chiefly the former, and numerous accidents resulted from their use. Parker observed arsenic in the urine twelve hours after the first application, which continued to be

detected during a period of eight or ten days. Toxic symptoms are recorded as occurring after the use of such strong pastes as the very old one, known as Frere Côme's, which is said to have cured Pope Gregory X of a cancer of the face. Maisoneuve mentions several cases in which its employment produced vomiting, precordial anxiety and other symptoms.

During the years 1834-1838 Canquoin of Paris reported the results which he had obtained from the use of a paste, the essential ingredient of which was chloride of zinc. He described four formulæ, as follows: (1) equal parts of zinc and flour; (2) zinc one part, flour two parts; (3) zinc one part, flour three parts; (4) zinc one part, muriate of antimony one part, flour 11/2 parts. Water from 20 to 30 drops for each formula. In 1838 a complete account of his results in 600 cases was published, in which the recurrences were given as 12 per cent. as compared with 75 per cent. after the use of the knife. Regarding the details of its application he says that formula (1) applied four lines in thickness for 48 hours destroys the parts to a depth of 1½ inches; that the same formula three lines in thickness applied for the same length of time acts only to about the depth of an inch. The depth to which the paste acts can, he says, with a little practice be regulated to the utmost nicety, depending upon its strength and the time it is applied. Plaster of paris may be substituted for flour, thus rendering it less delinquescent. The antimony was added in formula (4) to give it the same consistence as soft wax that it may be applied more uniformly over an unequal surface, such as is presented by an ulcerating growth. The advantage of the Canquoin paste over the arsenical preparations is attested by

the fact that, with few exceptions, chloride of zinc has been the effective ingredient of all pastes since used by surgeons and quacks. Parker (1867) says: "The chloride of zinc will effectually remove the chief evil attendant on the application of caustic remedies to the destruction of cancerous growthsthe amount of prolonged pain they occasion. may be applied with a degree of precision unobtainable by any other caustic; it destroys the tissue in direct relation with the thickness of the layer applied; it never runs or fuses; it destroys only those parts which it covers, and these it divides from the surrounding structures as cleanly as though they had been cut with a knife. The crust or scab formed by this caustic is hard, dense, and white; there is no sanguinous or other discharge produced by it. The eschar separates at the end of twelve or fourteen days, leaving a clean, healthy granulating surface underneath." In 1855 there appeared in the Dublin Quarterly Journal a method introduced by Llandolfi, chief surgeon of the Sicilian army and Clinical Professor of Cancerous Diseases in the Trinity at Naples, in which he used bromine, either alone or in combination with the chlorides of zinc, antimony and gold. The introduction of this method was not enveloped in any mystery, and Llandolfi's personality and method of presentation produced such a favorable impression in Paris, Germany and Vienna through which he traveled that his paste was tried by many and used with considerable success.

The efficiency of chloride of zinc is illustrated by the story Parker relates of a Dr. Fell, an American, who went to London and so successfully treated numerous cases of cancer that a certain number of patients at the Middlesex Hospital were placed at his disposal under the condition that he reveal and publish the composition of his remedy. This was ascertained to consist of equal parts of chloride of zinc and a decoction of sanguinaria canadensis, with enough flour to make a suitable paste. The hospital staff were apparently favorably impressed with the results. A little later, a Dr. Pattison, a London homeopathic physician, in association with an American from Louisiana, vaunted a remedy as a sure cure for cancer without the use of the knife or caustics, the results of which had evidently obtained for the exploiters considerable fame and for-Their refusal to reveal the nature of their remedy prevented its being tried at the Middlesex Hospital, but it was subsequently found to be a combination of chloride of zinc and hydrastis canadensis. Both Fell and Pattison administered the "novelty" in their preparations also internally, the latter dilution commensurate his in a with homeopathic traditions.

It is clear that the staff of the Middlesex Hospital, as well as surgeons of other hospitals, must have had innumerable experiences of this kind, but the results were evidently sufficient to make the use of caustics-in the earlier years of arsenic, and later, after the work of Canquoin, of the chloride of zinc, an important adjuvant to the use of the knife. Moore and De Morgan, of the Middlesex Hospital, the former of whom is known especially for his work in the development of the radical operation with the knife, used weak solutions of chloride of zinc-20, 30, 40 grains to the ounce of water, after their cutting operations in order to destroy cancer cells that may have been disseminated through the wound or the neighboring tissues. De Morgan was so well satisfied with the improved results from this method that he expresses the hope that it will be more extensively applied. They found that the use of these solutions made no appreciable difference with the primary healing of their wounds.

A disadvantage in the use of the chloride of zinc was its failure to satisfactorily remove the normal skin over the tumor site, and for this reason in part the alkaline caustics and mineral acids retained their vogue. The well-known Vienna paste consisted of five parts of potassium hydrate and six of quick lime. The "Filhos" caustic contained the same ingredients in different proportions, and was fused and run into leaden tubes like nitrate of silver or potassa fusa. Of the mineral acids, nitric acid was introduced by Rivallie (1850), in the form of monohydrated nitric acid made into a paste with scraped linen or charpie. For cancer of the servix uteri. Routh (1866) advocated to the Obstetrical Society of London the use of bromine—five grains to the ounce of spirits of wine. Tilt indicates that in his hands and others the application of the acid nitrate of mercury to a cancer of the uterus produced satisfactory results.

Reviewing the situation from the text-book literature of the sixth and seventh decades of the nineteenth century, we find Thomas (1869) expressing the opinion that, if it should be impracticable to remove completely a cancer of the cervix by amputation with the ecreseur, scissors, or the galvanocautery, it should be destroyed as completely as possible by the actual cautery, potassa cum calce, or one of the mineral acids. Erichson says: "The employment of caustics . . . requires neither knowledge of anatomy nor of operative surgery, and so they have always been popular with many who would hesitate to use the knife. In this country,

however, . . . they have not perhaps been legitimately employed to the extent they deserve. The chief argument in favor of caustics is that when cancers are thus destroyed they are less liable to relapse than when extirpated with the knife. There is, however, no positive proof of this before the profession; but it is not improbable that the chemical action of the caustics may extend so widely into neighboring structures as to destroy or render unproductive the cancer cells by which they are infiltrated, and on the development of which the local recurrence of the disease depends. Another advantage urged in favor of caustics is that enlarged glands are more likely to go down under their use than when the primary cancer is extirpated by the knife." In 1872 Bougard, a prominent Belgian surgeon, wrote most enthusiastically of the advantages in the use of caustics, stating that recurrences were less frequent than after the use of the knife. His formula, consisting largely of chloride of zinc with a small amount of arsenic, was used by numerous surgeons for several years. Willard Parker (1873), in a paper on cancer of the female breast, says: "In the superficial cancer of the breast it is very well to use caustics. The same thing might be said with regard to cancers upon the face. The treatment with caustics in that region is good surgery. When the tumor is situated to any extent below the surface, the idea of caustics is bad surgery." He referred to two cases of fatal poisoning from their use. In the discussion of this paper Fordyce Barker says: "Because of the general use of caustics by charlatans a great majority of the surgical world have been satisfied with regard to their uselessness. My own prejudices have always been against this method of treatment." As a result of

his observations in the St. Bartholomew's Clinic in London, the whole process seemed so revolting that he did not pursue his investigations further for some time. In 1870, however, he became so pleased with the work which he saw in the London Cancer Institute by Marsden that he applied this method of treatment successfully in two cases—one a cancer of the breast in which an operation with the knife had been refused, the other a cancer of the cervix uteri. He used the Marsden paste, which consisted of equal parts of arsenious acid and acacia. Sands, in his discussion of Parker's paper, said that he had had no experience with the use of caustics, but used the knife for the following reasons: (1) Nature of the tumor can not be determined prior to its removal; (2) now and then undoubtedly a malignant tumor is cured by operation: (3) expediency. J. Collins Warren says: "I have had little experience with the use of caustics. I find little difficulty in persuading patients to resort to more radical measures." About the face, to rodent ulcer, he preferred the use of the cautery. especially near the angle of the eye, because there resulted less of a scar, it being more difficult, he thought, to be economical of tissues with the knife. and more deformity resulted than when nature is allowed to borrow skin from all directions.

Stephen Smith (1880) describes his use of the anhydrous sulphate of zinc in the form of a powder, using a strong sulphuric acid paste for the removal of the skin. He says: "This remedy, though all but discarded by surgeons in the treatment of cancer, has a place in the therapeutics of cancer not yet accurately defined. It is one of the destructive measures which we may resort to, having capacities limited only by the possibilities of its application.

As ordinarily employed, its real virtues are not fairly nor adequately defined. We are advised, or rather permitted by authorities to apply caustics to ulcerated cancerous surfaces, the growth no longer being amenable to the knife. That is, caustics are recommended as a last resort, when the disease has taken such deep root that it is certain to prove fatal. If useful under such circumstances, may they not be far more serviceable at an earlier period? In my experience caustics judiciously selected and thoroughly and persistently applied give the best results of any method of treatment yet adopted." Dabney (1882) also reports favorable results from the use of this powder. Billroth (1889) expressed his preference for the use of the knife, but in very old, anaemic, or timid patients, thought caustics may be employed, and, if the treatment be continued until all the diseased portion is destroyed, the result will be favorable. "Physiologically," he says, "caustics would have some advantages; for it is supposable that the cauterizing fluid may enter the finest lymphatic vessels, and thus more certainly destroy the local disease. But this does not occur readily, because the tissue with which the caustic comes in contact instantly combines with it, and its further flow is thus prevented." For a caustic Billroth preferred chloride of zinc. Robinson (1892), in discussing the treatment of cutaneous epitheliomas, says that caustics with less scar remove more tissue than the knife. He used caustic potash and the formula of Bougard. Lewis (1893) used the Marsden paste for a number of years in the treatment of superficial cancer of the skin. Snow (1893) writes of the advantages obtained in the use of caustics on small superficial lesions, and in chronic epitheliomas, or rodent ulcers. He considered potassa fusa to be the most thorough and rapid, its action being instantaneously checked by the use of water, and causing no subsequent pain or shock. Parmenter (1894) says that it has not been proved whether caustics are better or worse than the knife, but he believes that the intelligent application of a proper caustic to easily accessible and definitely localized tumors, such as those of the skin, lip and external ear, has many advantages. Bulkley (1894) has found use for Marsden's paste, the potassa fusa, and Bougard's formula in early superficial malignant growths. Allen (1904) takes exception to White's statement that "the caustic treatment in the form of injections, pastes, and all other kinds of mixtures, rarely prove of any service, and usually only deceive and render more uncomfortable the existence of a patient. They have been discarded by almost all except charlatans." Impressive evidence of the value which the proper application of caustics may still possess in cancer therapy is furnished by the following words of Halsted (1907), in a paper on Carcinoma of the Breast: "I am indubitably convinced that the local and regionary recurrences after incomplete operations, which come with amazing rapidity when the knife has been used, are, to say the least, relatively late in making their appearance when chemical or actual cauterization has been employed. I have several times had to operate upon cancers which had been vigorously and repeatedly treated with caustics, and to note the comparatively admirable condition, the freedom from cancer premeation of the surrounding tissues and of the axillary nodes; whereas, after incomplete operations with the knife the local manifestations of recurrence were almost invariably deplorable and the prognosis, of course, invariably hopeless." He also says, "I doubt if any melanotic tumor of the skin should be removed with the knife."

From this review we learn that since the beginning of the nineteenth century chemical caustics were an increasingly valuable resource of all the noted surgeons in cancer therapy until Langston Parker (1867) in the Annual Address in Surgery. before the British Medical Association, showed that they had become a fair rival of the knife. In spite. however, of the undoubted success which attended their use during this period, we find that they were being applied less frequently by the skillful surgeons during the last quarter of the century. During the early years of the twentieth century their position in cancer therapy is not unlike that described by Young over one hundred years ago. "Caustic applications," he says, "were ushered in under the equivocal sanction of a nostrum, they were pursued as a nostrum, and then they were turned out as a nostrum. All regular inquiry has been withheld from the merits of the practice, and because it did not succeed in all things its efficacy was not allowed to any. Thus transferred from the irregulars to the regulars it was turned back to its original holders."

In the light of this history it may not be unprofitable to ask if they have a field for use at the present time?

Regarding the continuation of their use by the "original holders," we may hope that our educational propaganda and a more intelligent legislative restraint will ultimately solve that part of the problem. The question of renewal at the present time of the consideration of their efficacy by the educated surgeon naturally reverts to an estimate of their value when previously used and to the reason for their abandonment.

Their value as compared with the operation by the knife was apparently not satisfactorily defined at the time they were given up. No statistical data were available. We know that operations with the knife during a greater part of the nineteenth century were almost invariably incomplete and that the cures were few. Sands says, "Now and then a cure was accomplished." After the use of the chemical caustics, however, we have the evidence of numerous competent observers that the interval before recurrences appeared was often long, and there is much reason to believe that cures were more frequent than after operations with the knife. danger from poisoning was made a negligible factor by the very general substitution of zinc chloride for arsenic.

We do not find therefore that their value in the hands of competent surgeons was discredited, but the reason for their abandonment appeared to be in the new conception of the possibilities which scientific medicine furnished to the practical surgeon during the closing years of the century. Pathological anatomy was making an early and exact diagnosis more available, the results of bacteriological research promised to make primary mortality a negligible factor and primary healing of the wound a definite certainty, thus encouraging the surgeon to believe that ultimately the development of his technique would preclude the necessity of using chemical methods which were less attractive and extremely difficult to apply. Frequent and early recurrences could not obliterate the attractiveness of the primary result, and, until the past decade, sufficient solace could always be obtained in the idea that constitutional taint or heredity were compelling factors in the unfavorable progress of the disease.

The result is that the "salvage," as expressed by Clark in regard to uterine cancer is greater, but, owing to our failure to increase appreciably the number of patients applying for treatment in the earliest stages of the disease, the primary mortality has markedly increased, operative sequellæ are frequent, and recurrences are still discouragingly large. The words of Peterson (1912) are important, who, after expressing his strong belief in the radical operation for carcinoma of the uterus, says, "My added experience has not made me any more confident that the next patient I operate upon will either survive the primary operation or will ultimately be cured." Finally, there is the important fact that the availability of surgical skill sufficient to effect a respectable salvage is extremely limited—as much so as is that of radium.

We believe, therefore, that the evidence of the value of chemical caustics is sufficiently strong to justify a new study of their technical application and a discussion of the kind of cases in which they may be most efficiently applied. In so doing they may afford a valuable adjuvant to the use of the knife and become applicable to a number of well developed growths, the extirpation of which at the present time results in a high primary mortality and a high percentage of recurrences.

Regarding the educational propaganda of cancer, it seems to the writer that the study and application of all reasonable methods of treating cancer will be of aid in encouraging the public to seek early relief from competent hands. While anaesthesia and skill have diminished the dread of the knife, the fear of an operation still remains an important reason for the frequent delays in asking for advice.

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